ornithine translocase deficiency

Ornithine translocase deficiency is an inherited disorder that causes ammonia to accumulate in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if the levels become too high. The nervous system is especially sensitive to the effects of excess ammonia.

Ornithine translocase deficiency varies widely in its severity and age of onset. An infant with ornithine translocase deficiency may be lacking in energy (lethargic) or refuse to eat, or have poorly controlled breathing or body temperature. Some babies with this disorder may experience seizures or unusual body movements, or go into a coma. Episodes of illness may coincide with the introduction of high-protein formulas or solid foods into the diet.

In most affected individuals, signs and symptoms of ornithine translocase deficiency do not appear until later in life. Later-onset forms of ornithine translocase deficiency are usually less severe than the infantile form. Some people with later-onset ornithine translocase deficiency cannot tolerate high-protein foods, such as meat. Occasionally, high-protein meals or stress caused by illness or periods without food (fasting) may cause ammonia to accumulate more quickly in the blood. This rapid increase of ammonia may lead to episodes of vomiting, lack of energy (lethargy), problems with coordination (ataxia), confusion, or blurred vision. Complications of ornithine translocase deficiency may include developmental delay, learning disabilities, and stiffness caused by abnormal tensing of the muscles (spasticity).

Frequency

Ornithine translocase deficiency is a very rare disorder. Fewer than 100 affected individuals have been reported worldwide.

Genetic Changes

Mutations in the *SLC25A15* gene cause ornithine translocase deficiency.

Ornithine translocase deficiency belongs to a class of genetic diseases called urea cycle disorders. The urea cycle is a sequence of reactions that occurs in liver cells. This cycle processes excess nitrogen, generated when protein is used by the body, to make a compound called urea that is excreted by the kidneys.

The *SLC25A15* gene provides instructions for making a protein called a mitochondrial ornithine transporter. This protein is needed to move a molecule called ornithine within the mitochondria (the energy-producing centers in cells). Specifically, this protein

transports ornithine across the inner membrane of mitochondria to the region called the mitochondrial matrix, where it participates in the urea cycle.

Mutations in the *SLC25A15* gene result in a mitochondrial ornithine transporter that is unstable or the wrong shape, and which cannot bring ornithine to the mitochondrial matrix. This failure of ornithine transport causes an interruption of the urea cycle and the accumulation of ammonia, resulting in the signs and symptoms of ornithine translocase deficiency.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- HHH syndrome
- hyperornithinemia-hyperammonemia-homocitrullinemia syndrome
- hyperornithinemia-hyperammonemia-homocitrullinuria syndrome
- Triple H syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268540/

Other Diagnosis and Management Resources

- Baby's First Test
  http://www.babysfirsttest.org/newborn-screening/conditions/hyperornithinemia-hyperammonemia-homocitrullinuria-syndrome
- GeneReview: Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK97260
- GeneReview: Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217

- MedlinePlus Encyclopedia: Hereditary urea cycle abnormality
  https://medlineplus.gov/ency/article/000372.htm
- National Organization for Rare Disorders (NORD) Physician Guide: Urea Cycle Disorders
  http://nordphysicianguides.org/urea-cycle-disorders/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Hereditary urea cycle abnormality
  https://medlineplus.gov/ency/article/000372.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Mitochondrial Diseases
  https://medlineplus.gov/mitochondrialdiseases.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Ornithine translocase deficiency syndrome
  https://rarediseases.info.nih.gov/diseases/2830/ornithine-translocase-deficiency-syndrome

Educational Resources

- Disease InfoSearch: Ornithine translocase deficiency syndrome
  http://www.diseaseinfosearch.org/Ornithine+translocase+deficiency+syndrome/5413
- Genetics Education Materials for School Success (GEMSS)
  http://www.gemssforschools.org/conditions/urea-cycle/default
- MalaCards: hyperornithinemia-hyperammonemia-homocitrullinemia syndrome
  http://www.malacards.org/card/hyperornithinemia_hyperammonemia_homocitrullinemia_syndrome
- Orphanet: Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=415

Patient Support and Advocacy Resources

- Climb National Information Centre for Metabolic Diseases (UK)
  http://www.climb.org.uk/
- National Urea Cycle Disorders Foundation
  http://www.nucdf.org/
- Urea Cycle Disorders Consortium
  http://www.rarediseasesnetwork.org/cms/ucdc/Learn-More/Disorder-Definitions

GeneReviews

- Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK97260
- Urea Cycle Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1217

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22ornithine+translocase+deficiency%22+OR+%22Amino+Acid+Metabolism%2C+Inborn+Errors%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ornithine+translocase+deficiency%29+OR+%28HHH+syndrome%29+OR+%28hyperornithinemia-hyperammonemia-homocitrulllinemia+syndrome%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- HYPERORNITHINEMIA-HYPERAMMONEMIA-HOMOCITRULLINURIA SYNDROME
  http://omim.org/entry/238970

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